REMARKS

Reconsideration of the present application, as amended, is respectfully requested. The present application, as amended, includes claims 1-4, 6-20 and 23-26, pending and under consideration.

As a preliminary matter, a number of amendments have been made to the specification for clarification or to correct typographical errors. The amendments to page 31, line 17 and to page 33, line 13 are supported by Figure 1, which shows that the transferrin iron binding capacity is 234 µg/dl rather than 225 µg/dl.

The amendments to page 23, line 4; page 25, line 2; and page 31, line 3 all correct typographical errors in the specification. The amendments to page 18, line 7; page 28, line 3; and page 32, line 9 are for purposes of clarification.

In the outstanding Office Action, claims 13-16 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Ash '141 and Callingham et al. '411. In traversal of this rejection, Applicant submits that the Examiner has failed to establish a prima facie case of § 103(a) obviousness because there is no suggestion or motivation to modify the references or to combine their teachings.

It is first respectfully submitted that the Action mischaracterizes both Callingham et al. '411 and Ash

'141. It is stated on page 2, paragraph 2 of the Action that Callingham et al. teaches ferrous gluconate administered intraperitoneally. Applicant respectfully disagrees with this characterization of Callingham et al., and submits that this reference is directed to the administration of compositions to a patient buccally and/or nasally. While the reference mentions the use of iron gluconate experimentally as a comparison chemical to the preferred iron:maltol complex (See Examples 4 and 5, columns 13-14), the iron gluconate is not administered intraperitoneally. In Examples 4 and 5, procedures are described in which an iron gluconate sample (and, alternatively, a number of other comparative samples) is passed into the duodenum, or small intestine, of a rat and a cat, respectively. The sample enters the small intestine via a cannula passing through a small incision in the intestinal wall. After a given period of time, the organ is harvested and assayed to determine its iron content.

The passage of a compound into a duodenum does not constitute intraperitoneal administration, and therefore, the Action in this respect mischaracterizes the Callingham et al. reference. The term "intraperitoneal administration" is well understood by persons skilled in the relevant field to refer to the introduction of a

composition into a patient's peritoneal cavity, i.e., the anatomical space within the peritoneal membrane, which lines the abdominal wall, and exterior to the organs residing in the abdomen, including, for example, the intestines. Therefore, a reference which describes introducing a sample into a duodenum does not teach intraperitoneal administration, as this term is used and understood in the art and as asserted in the Action.

It is also submitted that the Ash '141 reference is mischaracterized in the Action, wherein it is stated at page 2, paragraph 2 that "Ash teaches internal administration of the additional ions of claim 16." The Ash reference in fact discloses a dialysis composition for an extracorporeal blood treatment system, and has nothing to do with "internal administration" of a dialysate. It is well known in the relevant field that extracorporeal blood treatment, the subject of Ash '141, involves the removal of blood from a patient. The blood, exterior to the patient, is then passed in contact with a membrane, which membrane is also contacted, opposite the blood, with a dialysate composition such as that described in Ash '141. Therefore, Ash does not teach internal administration of a dialysate.

To establish a prima facie case of obviousness, the Examiner must identify in the prior art some teaching or

suggestion to combine the cited references. "Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art." (citations omitted). Manual of Patent Examining Procedure ("MPEP") § 2143.01.

It is submitted that the Action is devoid of any explanation of how the cited references, or any other teaching in the prior art of record, suggest the modifications of the references that the Examiner has asserted is obvious. The Examiner asserts that, "Nothing unobvious can be seen in combining and administering said ingredients for their expected additive effects." It is submitted, however, that there is no suggestion to combine an iron complex with a dialysate composition in accordance with the invention and, indeed, there are no expected additive effects. As shown in the specification, the art teaches away from introducing iron to a patient in this manner, and "it is widely believed that soluble iron complexes are unacceptable iron delivery agents, this belief being based upon a fear of the toxicity of free iron in blood." (Specification page 7, lines 5-8). Therefore, any expected additive effect of combining an

inventive iron complex with a dialysate in accordance with the invention would be that the resulting composition would be unacceptable for dialysis.

The only suggestion to provide and use a dialysate comprising an iron complex is provided by the present application. "When prior art references require selective combination . . . to render obvious a subsequent invention, there must be some reason for the combination other than the hindsight gleaned from the invention itself." Uniroyal v. Rudkin-Wiley, 5 USPQ 2d 1434, 1438 (Fed.Cir. 1988) (quoting Interconnect Planning Corp. v. Feil, 227 USPQ 543,551 (Fed.Cir. 1985)). Some teaching in the prior art as a whole must suggest the desirability, and thus the obviousness, of making the combination. Lindemann Maschinenfabrik GmbH v. American Hoist and Derrick Co., 221 USPQ 481, 488 (Fed.Cir. 1984). It is respectfully submitted that there is no such teaching or suggestion in the prior art for making the combination proposed by the Examiner.

Without the benefit of hindsight gained from viewing the present application, one having ordinary skill in the art would recognize that both Callingham et al. and Ash, in fact, disclose significantly different methods, using significantly different compositions, to achieve significantly different results. Furthermore, at the time

of the invention, a skilled artisan would not have selected an ingredient from an obscure comparative example in the Callingham et al. reference, and placed the ingredient in a dialysate. Indeed, nobody, save the present inventor, suggested that this be done, even in view of the difficulties that had been encountered in the prior art of delivering iron to iron-deficient patients (See pages 2-6 of the specification).

The Examiner has simply used Applicant's claims as a recipe to pick and choose isolated facets out of diverse art. "The result is that the claims were used as a frame, and individual, naked parts of separate prior art references were employed as a mosaic to recreate a facsimile of the claimed invention." W.L. Gore & Assoc. Inc. v. Garlock, Inc., 220 USPQ 303,312 (Fed. Cir. 1983). At no point has the Examiner explained why that mosaic would have been obvious to one skilled in the art at the time of the invention, or what there was in the prior art that would have suggested this combination. "To imbue one of ordinary skill in the art with knowledge of the invention in suit, when no prior art reference or references of record convey or suggest that knowledge, is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher." Id. at 312-13. Because there

is no suggestion of combination to be found within the cited references, Applicant respectfully submits that claims 13-16 are allowable over the references of record and requests that the rejection under 35 U.S.C. § 103 be withdrawn.

In addition to the above, there are further reasons that the § 103 rejection should be withdrawn. For example, to establish a prima facie case of obviousness, the prior art reference (or references when combined) must teach or suggest all the claim limitations. (See MPEP § 2142). A limitation recited in claims 13-15 of the present application is that a dialysate is introduced "into a patient's peritoneal cavity." Neither of the cited references, taken for what they do, in fact, disclose, nor a combination of the references, teaches or suggests the introduction of a dialysate or any other composition into a patient's "peritoneal cavity" as that term is used and understood in the field of dialysis.

Callingham et al. discloses delivery of iron preparations buccally, nasally or, for experimental purposes, intestinally, but makes no reference to intraperitoneal administration of a composition as that term is used and understood in the relevant field. However, introduction of a composition into a buccal cavity, into a nasal cavity or into a duodenum does not

constitute introduction into the "peritoneal cavity." Further, Ash discloses the extracorporeal treatment of blood and makes no suggestion of internally administering a dialysate composition. It is therefore respectfully submitted that the Examiner has failed to establish a prima facie case of obviousness of claims 13-15 because the cited references, taken alone or in combination, do not teach or suggest each limitation of claims 13-15.

Claims 1-23 were also rejected in the outstanding Office Action under 35 U.S.C. § 112, first paragraph as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The Action asserts that claims 1-19 and 21-23 "are too broad in not reciting proportions of ingredients and/or amounts administered"; and that claims 1-8, 10, 11 and 13-23 "are broader than warranted by the disclosure of a single iron compound."

To expedite the allowance of claims, Applicant has introduced new claims 24-26 into the application, these claims reciting specific compositions and concentrations. For the reasons stated below, however, it is submitted that claims 1-4, 6-20 and 23 are allowable as amended.

Applicant respectfully traverses the rejection under 35 U.S.C. § 112, first paragraph, and submits that a person of ordinary skill in the art at the time Applicant filed his application for patent, in view of the specification, would have been able to practice the invention by selecting an appropriate iron complex, by selecting appropriate proportions of ingredients, and by administering an appropriate amount of dialysate to a patient. "The test of enablement is whether one skilled in the art could make or use the claimed invention from the disclosure in the patent coupled with information known in the art without undue experimentation." MPEP § 2164.01. It is not required that the inventor list every conceivable composition that falls within the scope of a given claim, but rather, that the invention be described in such a manner that a person of ordinary skill in the art could determine, without undue experimentation, whether a composition falls within the scope of a claim.

With respect to the selection of an iron complex in accordance with the invention, the specification describes the term "iron complex," or "complex," in great length, thereby providing a person skilled in the art with a roadmap to identify compositions that fall within the meaning of these terms as claimed. Applicant respectfully disagrees with the statement in the Action that the

specification constitutes a "disclosure of a single iron compound." Rather, the specification fully describes a class of compounds, including the distinguishing features of these compounds and detailed descriptions of how the compounds may be identified. The specification also provides examples of compositions which fall within the class. In addition to ferrous gluconate, the specification states on page 27 that "suitable anions for iron complexes of the invention include, for example, gluconate, sulfate, fumarate, citrate and succinate."

It is stated on page 28 of the specification that:

> Complexes selected for use according to the invention may be identified . . . by their molecular weight, by their degree of solubility in an aqueous medium and by their ability to remain tightly complexed under conditions of the invention.

The specification, therefore, describes a complex in accordance with the invention in terms of size (i.e., molecular weight), solubility and the ability to remain complexed, but not agglomerated, in solution.

With respect to the size of the complex, the specification states on page 23, in terms readily understood by those skilled in the art, that a complex used in accordance with the invention "has a molecular size and, correspondingly, a molecular weight, which imparts advantageous properties with respect to diffusion of the complex through a dialysis membrane." It is also

readily understood that a wide variety of dialysis membranes exist which are more or less restrictive of the size of molecules that are able to diffuse therethrough. Thus, it is incumbent upon, and well within the purview of, a skilled artisan to determine which complex is best suited to a given membrane. Further guidance is given on page 21 of the specification, where it is stated that, "In intraperitoneal dialysis techniques, just as in hemodialysis techniques, a smaller iron complex will move more readily from the dialysate into the patient's blood than will a larger complex.

Inventive iron complexes are also described in terms of solubility. As stated on page 23 of the specification, a complex encompassed by the present invention is one which "is soluble in an aqueous medium . . . [and] the solubility of a given iron complex according to the present invention must be such that the concentration of the complex in a dialysate solution may be achieved which enables the desired level of iron delivery to the patient." How to determine a given patient's iron needs is well within the purview of a skilled artisan, and is described in the specification (See pages 23-24). It is also within the purview of a person skilled in the art to thereby determine the degree of solubility needed to achieve a proper level of delivery. A skilled artisan can

also, without undue experimentation, determine whether a given composition exhibits this level of solubility.

The specification also describes a complex on pages 21-22 of the specification, as an "association between two or more ions to form a relatively low molecular weight non-polymeric composition which exists singly under a given set of conditions. . . [Inventive complexes do not undergo] association or agglomeration [with other] primary complexes into a large macromolecule." As the specification sets forth multiple examples of iron complexes and also fully describes compounds which fall within the scope of the invention, Applicant respectfully traverses the rejection of claims 1-8, 10, 11 and 13-23 in the Action under 35 U.S.C. § 112, first paragraph.

Applicant also disagrees that claims 1-19 and 21-23 are too broad in not reciting proportions of ingredients and/or amounts administered. It is submitted that a wide variety of concentrations of ingredients are contemplated by the invention and it is within the purview of a skilled artisan, in view of the specification, to select proportions suitable or advantageous for a given situation. It is further submitted that the amount of dialysate administered to a patient is well within the purview of a skilled artisan.

With respect to proportions of ingredients, it is stated on pages 23-24 of the specification that:

> The particular concentration of iron complex to be dissolved in a dialysate according to the present invention is dependent upon the amount of iron desired to be transferred to the patient's blood. For example, the amount of iron desired to be transferred in the case of an anemic patient is associated with the known blood building requirements of the patient. In other words, to determine the desired concentration of the iron complex in the dialysate, it is first calculated how much iron the patient needs for building blood cells. The complex will transfer to the patient at a controlled, definable rate, since the iron complex does not exist naturally in the blood. As is readily understood by one skilled in the art, a higher concentration of iron complex would be needed in peritoneal dialysis techniques than that which would be needed in extracorporeal hemodialysis techniques due to differing rates of diffusion with respect to the respective membranes and due to the lower daily volume of dialysate used in peritoneal dialysis. Preferred concentrations in a given situation may be readily determined by a skilled artisan with minimal experimentation.

It is also readily understood that the size of an inventive complex has a significant effect upon the optimal concentration in a given dialysate. For example, where a relatively large complex is used, it is understood that a higher concentration will be needed to exhibit the same degree of iron delivery as a smaller complex at a lower concentration. Therefore, an optimal concentration for delivery of a relatively large iron complex to a patient having a high level of iron deficiency differs significantly from an optimal concentration for a patient having a lesser deficiency and where a relatively small

complex is used. Therefore, recitation of concentrations in each claim of the present application would be unduly limiting, and would not provide the scope of protection to which the present inventor is entitled.

While the amount of dialysate administered to a patient during a given treatment is also within the purview of a skilled artisan, guidance for this is also found in the specification. Particularly, for hemodialysis, page 14 of the specification states that "dialysate flow rates are usually set at about 500 ml/min [and a] dialysate volume of about 120-200 liters is typically used per dialysis treatment." For peritoneal dialysis, pages 18-19 of the specification states that "approximately 2 liters of a sterile, nonpyrogenic, and hypertonic solution of glucose and electrolytes are instilled via gravity flow into the peritoneal cavity of a patient through an indwelling catheter, typically 4 times per day." For automated peritoneal dialysis, page 19 of the specification states that "about 10-15 liters of dialysate are automatically exchanged overnight and 2 liters remain in the peritoneal cavity during the day for a 'long dwell' exchange." It is readily understood that alternate forms of peritoneal dialysis are also contemplated by the invention, and appropriate amounts of dialysate are well within the purview of a skilled artisan

for a wide variety of protocols. For the reasons stated, Applicant respectfully submits that the rejection of claims 1-23 under 35 U.S.C. § 112, first paragraph, is overcome.

Claims 1, 5, 18 and 20 are rejected under 35 U.S.C. § 112, second paragraph. It is stated in the Action that claims 1 and 5; and claims 18 and 20 are duplicate claims. With regard to claims 1 and 5, the cancellation of claim 5 overcomes this rejection. With respect to claims 18 and 20, Applicant submits that claim 20 clearly includes limitations not set forth in claim 18, specifically, concentration limitations. Applicant therefore respectfully requests that this rejection be withdrawn.

In view of the foregoing, Applicant submits that the present application, as amended and containing claims 1-4, 6-20 and 23-26 is in condition for allowance and that the rejections asserted in the outstanding Action should be withdrawn. Action to that end is therefore requested.

Respectfully submitted,

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